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Abstract

Development of a Tubular Bacteriophage-Based Vaccine Platform that Induces an Immune Response in Mice †

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Abstract: Current vaccines against infectious diseases have primarily relied on attenuated or inactivated pathogens. However, self-assembled, virus-based nanoparticles (VNPs) are noninfectious multiprotein structures regarded as safe vaccine platforms for an efficient foreign antigen display within a host immune system. Currently, there is a low diversity of self-assembled, rod-shaped VNPs. Additionally, there is no information regarding the generation of tailed-bacteriophage nanotubes in yeast and their immunogenicity in mice. Here, we developed a novel tubular VNP-based vaccine platform utilizing a yeast-synthesized recombinant tail tube gp39 protein from bacteriophage vB_EcoS_NBD2 (NBD2). The diameter of these extremely flexible polytubes was ~12 nm, while the length varied from 0.1 μm to >3.95 μm. In this study, the immunogenicity of polytubes formed by the recombinant gp39 protein and the elicited antibody response were tested. The tubular structures formed by the recombinant gp39 protein were immunogenic in mice, although the addition of Freund's adjuvant enhanced the anti-gp39 antibody response compared to the use of tubular structures alone. To further examine the applicability of novel polytubes as a carrier for foreign epitopes, the carboxy-terminal region within the gp39 protein was identified, allowing insertion of six histidine residues with no effect on the recombinant protein synthesis or structure self-assembly. This genetic insertion of a foreign epitope within the surface-exposed gp39 domains resulted in a repetitive display of the insert on the surface of NBD2 tail tube-originated polytubes. The combination of a repetitive, highly ordered display of foreign epitopes as well as tubular shape of nanoparticles can greatly enhance the immune response. Although more studies are needed, the flexible and extremely long polytubes formed by the recombinant tail tube gp39 protein represent a new potential platform for presenting target sequences on the exterior surface of the nanotubes.

Keywords: bacteriophage-based particles; self-assembly; tubular structure; epitope display; immunogenicity